Technological Advancements in Biomedicine for Healthcare Applications

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Chapter 1

Description of and Applications for a Motion Analysis Method for Upper Limbs

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In daily life, we often perform activities with the upper limbs. Various motions of the upper limbs are required when performing activities of daily living (ADL), such as eating, dressing, grooming, or operating a home appliance. When problems first occur with human upper limb motions, a detailed analysis should be performed to determine where the difficulty with motion exists and to identify conditions under which we can perform these activities more easily and efficiently. Next, adjustments should be made to the activity or to the interface design of appliances to reduce the difficulty posed by the problematic motion. In this chapter, the methods of motion analysis for human upper limbs are explained and the effective method of utilization is shown. A case study is also provided to demonstrate the analysis of the pointer operation for cerebral palsy patients using a laptop PC which operates by a graphical user interface operating system (GUI OS) to provide a barrier-free approach. Additionally, an applied case study of the motion analysis methods for human upper limbs is shown, and the countermeasure to develop an effective pointer operation for cerebral palsy patients is discussed.

Chapter 2

An EMG Control System for an Ultrasonic Motor Using a PSoC Microcomputer

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The author investigated the possibility of developing a myoelectric elbow prosthesis powered by an ultrasonic motor. Ultrasonic motors have some features that make them uniquely suited to powering prosthetics: they deliver high torque under low-speed operation, they are compact in size and they produce no electromagnetic noise. Typically, the threshold-level of an EMG (electromyogram) is adopted as the method for myoelectrically controlling prostheses using a microcomputer. However, this method is not suitable for every prosthesis. Here, the author proposes an EMG control system for a myoelectric elbow prosthesis that uses a PSoC microcomputer combined with an accelerometer to create an ultrasonic motor. The chapter shows that the EMG control system developed by the author effectively controlled the ultrasonic motor.
Chapter 3
A New, Non-Invasive in vivo Optical Blood Glucose Measurement Technique Using Near-Infrared Radiation ("Pulse Glucometry") and a Proposal for "Pulse Hemo-Photometry"

Blood Constituent Measurements .................................................................................................................. 18

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Takehiro Yamakoshi, Kanazawa University, Japan
Kenta Matsumura, Kanazawa University, Japan
Kosuke Motoi, Hirosaki University, Japan
Ken-ichi Yamakoshi, Kanazawa University, Japan

A recently proposed optical method for a non-invasive in vivo blood glucose level (BGL) measurement named "pulse glucometry" is introduced. This method is based on near-infrared living body spectroscopy to accurately obtain blood information. The remarkable feature of the method is the measurement of both the total transmitted radiation spectra in wavelength $\lambda$ ($I_\lambda$) and the cardiac-related pulsatile component ($\Delta I_\lambda$). When $\Delta I_\lambda$ is superimposed on $I_\lambda$, the differential optical density ($\Delta OD_\lambda$), which includes only arterial blood information, is obtained, thus avoiding interference from living tissues other than arterial blood. Another feature is the ability to measure the differential optical density ($\Delta OD_\lambda$) in multiple wavelengths to avoid interference from blood constituents other than the target blood chemical (glucose).

Chapter 4
Biomedical Application of Multimodal Ultrasound Microscope ................................................................ 27

Yoshifumi Saijo, Tohoku University, Japan

High frequency ultrasound imaging has evolved from the classical acoustic microscope to the multimodal ultrasound microscope, which is available for quantitative C-mode, surface acoustic impedance mode, and three-dimensional (3D)-mode imaging. This evolution has realized both quantitative parametric imaging and easier observation. Quantitative C-mode represents two-dimensional sound speed distribution and is realized by frequency-domain analysis of a single pulse by a high-speed digitizer. Because the square of sound speed is proportional to tissue elasticity, sound speed imaging provides biomechanical information about the tissue. Surface acoustic impedance mode has been used to image fresh brain tissue. High-frequency 3D-mode imaging has been used to visualize the 3D structure of dermis sebaceous glands.

Chapter 5
Biomedical Information Processing and Visualization for Minimally Invasive Neurosurgery ............... 36

Hongen Liao, The University of Tokyo, Japan & Tsinghua University, China

This chapter demonstrates a particular application of biomedical information processing and visualization techniques for minimally invasive diagnosis and therapy in neurosurgery. Computer-assisted surgical navigation provides surgeons valuable information on the precision location of surgical targets and critical areas, as well as the positions of surgical instruments. However, most navigation systems use pre-/intra-operative images, which are displayed on a two-dimensional (2D) display situated away from the surgical field. These setups force the surgeon to take extra steps to match navigation information on the display with the actual surgical target of the patient. Two typical medical information-based navigation systems for neurosurgery are described in this chapter. First, an integration system with fluorescence-based intra-operative diagnosis and laser ablation-based, high-precision, minimally invasive treatment is introduced. Second, an autostereoscopic image-guided surgical system developed for minimally invasive neurosurgery is discussed. The autostereoscopic image and corresponding augmented real-
ity with three-dimensional (3D) image overlay have been used in open magnetic resonance imaging (MRI)-guided neurosurgery. These techniques enable intra-operative visualization of surgical targets for precision tumor resection.

Chapter 6
Image Fusion Method and the Efficacy of Multimodal Cardiac Images ................................................. 47
Tadanori Fukami, Yamagata University, Japan
Jin Wu, Chiba University Center for Forensic Mental Health, Japan

Currently, there is no single type of medical image that provides an indispensable tool for clinical diagnosis and treatment. Rather, different imaging devices are used for different diseases. Each imaging device has both advantages and disadvantages. To provide a more complete picture and to improve accuracy in diagnosis, techniques that combine images taken by different imaging modalities have recently been used more in clinical practice. In addition, researchers continue to develop these techniques. Previously, images taken by different devices at different times were integrated using image processing techniques. After the development of hybrid imaging devices that can connect two kinds of devices, complicated processing by software was reduced. In this chapter, the authors review some representative imaging modalities that are commonly used as diagnostic tools and discuss the use and efficacy of image fusion techniques for clinical use.

Chapter 7
The Development of a Quantitative Method for the Detection of Periarticular Osteoporosis Using Density Features within ROIs from Computed Radiography Images of the Hand .................. 55
Seiichi Murakami, Kyushu Institute of Technology, Japan & University of Occupational and Environmental Health, Japan
Hyoungseop Kim, Kyushu Institute of Technology, Japan
Joo Kooi Tan, Kyushu Institute of Technology, Japan
Seiji Ishikawa, Kyushu Institute of Technology, Japan
Takatoshi Aoki, University of Occupational and Environmental Health, Japan

Periarticular osteoporosis of the hands and feet is one of the major diagnostic criteria for rheumatoid arthritis (RA). However, a quantitative method to detect periarticular osteoporosis using radiographs has not been reported. In this chapter, the authors propose a quantitative method for the detection of periarticular osteoporosis using density features of regions of interest (ROIs) from computed radiography (CR) images of the hand. The proposed method measures the density features of ROIs using histogram analysis, co-occurrence matrices, Fourier analysis, and the extraction of line components. Periarticular osteoporosis is detected using a discernment function based on these measurements. The sensitivity and specificity of the proposed method was assessed using 188 joints from 17 cases, including 6 normal cases (without periarticular osteoporosis) and 11 abnormal cases (with periarticular osteoporosis). The sensitivity of the method was 88.9%, and the specificity was 98.1%. Therefore, the authors consider this method to be potentially useful to radiologists for detecting periarticular osteoporosis in the hands.

Chapter 8
Construction of Digital Statistical Atlases of the Liver and their Applications to Computer-Aided Diagnosis .......................................................... 68
Yen-Wei Chen, Ritsumeikan University, Japan

Digital atlases of the human anatomy are a new and hot topic in medical image analysis. The basic idea of the digital atlas is to capture the variability of an organ’s location, shape, and voxel intensity (texture) from a training set. In this chapter, the authors present current progress toward constructing digital
atlases of the liver and their applications to liver segmentation and diagnosis of hepatic disease. They also introduce a new mathematic framework (generalized N-dimensional principal component analysis) based on multi-linear algebra for medical volume analysis.

Technology in Rehabilitation

Chapter 9
Functional Electrical Stimulation (FES) Control for Restoration and Rehabilitation of Motor Function
Takashi Watanabe, Tohoku University, Japan
Naoto Miura, Tohoku University, Japan

Functional electrical stimulation (FES) has been studied and clinically applied to restoring or assisting motor functions lost due to spinal cord injury or cerebrovascular disease. Electrical stimulation without control of functional movements is also used for therapy or in rehabilitation training. In recent years, one of the main focuses of FES studies has been its application for rehabilitation of motor function. In this review, the authors first present the basics of applying electrical stimulation to the neuromuscular system for motor control. Then, two methods of FES control are discussed: controllers for FES based on feedback error learning (FEL) and on cycle-to-cycle control of limb movements. The FEL-FES controller can be practical in FES applications that need to control the musculoskeletal system that involves various nonlinear characteristics and delay in its responses to electrical stimulation. The cycle-to-cycle control is expected to be effective in controlling repetitive movements for rehabilitation training. Finally, a study on ankle dorsiflexion control during the swing phase using an integrated system of FES control and motion measurement with wearable sensors for rehabilitation is presented.

Chapter 10
Human-Friendly Mechatronics Systems with Functional Fluids and Elastomers
Takehito Kikuchi, Yamagata University, Japan

Safety for humans is one of the most important issues for systems in which humans and machines coexist. Man has developed human-friendly devices using functional materials (electrorheological fluids (ERF), magnetorheological fluids (MRF), and magnetic-field sensitive elastomers (MSE)) and applied them to several types of robots and mechatronics devices for health care, life support, and the evaluation of human functioning. In this chapter, projects related to human-machine coexistent systems and functional materials are presented and classified according to their applications.

Chapter 11
A Strength Training Machine with a Dynamic Resistance Control Function Based on Muscle Activity Level
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A unique machine for strength training is introduced in this chapter. This training machine dynamically controls the amount of electronically generated resistance to provide a varying resistance force that follows a desired pattern during the exercise. This pattern or trajectory of desired muscle activity levels can be easily set prior to exercise through an interactive panel on the computer screen. It is predicted that this technology could facilitate more safe and effective strength training. The methodology for the muscle activity-based resistance control and the mechanism of the proposed system are detailed using a leg press prototype machine. The unique training features offered by the prototype are presented with data recorded from demonstrations and experiments.
Chapter 12
Medical Manipulators for Surgical Applications

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Great advances have been made over the last decade with respect to medical manipulators for surgical robots. Although they cannot replace surgeons, they can increase surgeons’ abilities to perform surgeries with greater therapeutic effectiveness. These advanced surgical tools have been implemented in complex, precise, repetitive, and difficult surgeries. This chapter reviews medical manipulators used in surgical applications. At present, several kinds of medical manipulators have been developed to perform a variety of surgical procedures and can be classified into different categories. Here, the authors discuss general design principles and summarize and classify medical manipulators based on joint category and level of autonomy, with illustrations of applications. Finally, a brief synopsis is provided.

Chapter 13
Design of and Experimentation with a Walking Assistance Robot

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Yi Lei, Harbin Engineering University, China

To help patients with lower limb disabilities walk, a robot was designed to help train patients to stand up. An experimental prototype was developed, and experiments to train patients stand up and walk were performed using this robot. The results show that the robot can help patients to stand from a sitting position, which is the purpose of standing-up training. At the same time, the standing-up mechanism can coordinate with the walking assistance mechanism in the walking training mode, allowing the robot to help patients to perform rehabilitation walking training. The justification of the mechanism design was demonstrated, and thus, the robot can be used for standing-up training and walking training.

Chapter 14
Neurosurgical Operations Using Navigation Microscope Integration System

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Nobuyuki Kawai, Kagawa University, Japan
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The use of intraoperative navigation systems in neurosurgery has increased rapidly. The Neuronavigation Microscope Integration (NMI) system consists of a microscope (Zeiss, Germany) combined with the StealthStation (Medotronic, U.S.A.) including light emitting diodes, a dynamic reference frame with light emitting diodes, an optical digitizer with camera array and a computer workstation. The aim of this study was to determine the usefulness of the NMI system for neurosurgical operations. Between April 2003 and March 2011, the authors used the NMI system in 367 patients undergoing neurosurgical operations at Kagawa University Hospital. Because the navigational informations could be superimposed onto the microscope view, accurate locations of tumor and normal anatomical structures could be obtained before skin incision. During the operations, the surgeons did not need to turn away from the surgical field or to use a bulky pointer. Catheter applications along the tumor borderline guided by the NMI system could be useful for glioma surgery. Deep seated lesions including intraventricular or intra-axial tumors could be removed through accurate and minimal corticotomy. For transsphenoidal surgery, pituitary tumors...
could be safely removed without X-ray imaging. For the skull base surgery, the navigational information was not affected by the brain shift during the operations. The registration assessment deviations were within 2 mm and the real anatomical deviations were within 3 mm. The authors’ findings suggest that the NMI system can provide valuable and reliable intraoperative navigational informations during neurosurgical operations.

Chapter 15
Wearable Power Assist Robot Driven with Pneumatic Rubber Artificial Muscles

Toshiro Noritsugu, Okayama University, Japan

A wearable power assist robot to enhance muscular power using actuators is sought after for welfare applications, et cetera. Pneumatic rubber artificial muscles are seen as some of the more useful wearable actuators because of their inherent light weight and softness. In this chapter, the author first outlines the current state of the research and development of this kind of robot before introducing some pneumatic rubber artificial muscles developed in the author’s laboratory. The chapter then moves on to explain about the wearable power assist devices driven with these artificial muscles; both the exoskeleton type and the non-exoskeleton type are wearable power assist devices. These power assist wear could be considered ideal as a wearable and comfortable power assist device.

Chapter 16
Bone-Conducted Ultrasonic Perception: An Elucidation of Perception Mechanisms and the Development of a Novel Hearing Aid for the Profoundly Deaf

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Although the mechanisms involved remain unclear, several studies have reported that bone-conducted ultrasounds (BCUs) can be perceived even by those with profound sensorineural deafness, who typically hardly sense sounds even with conventional hearing aids. Interestingly, these patients appear to perceive BCUs as well as subjects with normal hearing. The perception of BCUs by the profoundly deaf has been objectively proven using magnetoencephalography (MEG). Furthermore, the author has identified both the psychological characteristics and the neurophysiological mechanisms underlying the perception of BCUs using psychophysical, electrophysiological, and physical approaches. In addition, the author has developed a BCU hearing aid (BCUHA) for the profoundly deaf. Remarkable results have already been achieved with this device, which enabled 42% of the profoundly deaf subjects in the trial to perceive some sort of sound and 17% of them to recognize simple words. These results suggest the feasibility of this device, but additional development and improvements are needed.

Biomedical Robotics for Healthcare
organ tissue via forceps because they cannot directly touch the tissue. The evaluation of force-based skill is critical in the judgment of whether a person has adequate manipulation skills to conduct surgery procedures. Currently, simulation training in minimally invasive surgery is a required component of general surgery residency training. A primary obstacle in the development of a training simulator with a haptic feedback capability is its high cost. This chapter addresses two research issues that must be integrated in the development of a cost-effective haptic training system: the challenge of skill evaluation during laparoscopic surgery by measuring the force applied to forceps, and a novel haptic display based on a haptic augmented reality (AR) technique.

Chapter 18
Small Medical Robot .............................................................. 170
Makoto Nokata, Ritsumeikan University, Japan

This chapter describes the development of a small medical robot that remains in the abdominal cavity to monitor sites of medical interest and discusses robot travel operations and specifications. A long, narrow piece of ferromagnetic material was placed inside the robot, and an external magnetic field was used to set the robot in motion. The author developed a prototype robot and conducted experiments in order to verify the proposed concept and the principle of steering the robot. In vivo experiments in rabbits demonstrated that solenoids produce sufficient magnetic force to enable the robot to travel through the abdominal cavity, verifying the motion principles. The experiments also confirmed the appropriate shape of the robot, and friction between the robot and the organs and abdominal wall was measured. A modified prototype of the robot was then used to conduct clinical experiments in the rabbit model; a surgeon operated the XYZ axis stages in order to adjust the position of the subject for the experiment and moved the robot to the liver. Robot travel from the insertion point to the liver was verified on X-rays. The long distance was possible due to the improved shape and the use of accurate magnetic field imaging.

Chapter 19
Functional Electrical Stimulation Based on Interference-Driven PWM Signals for Neuro-Rehabilitation ......................................................... 180
Hiroshi Yokoi, The University of Electro-Communications, Japan
Ryu Kato, The University of Electro-Communications, Japan
Takashi Mori, The University of Electro-Communications, Japan
Osamu Yamamura, University of Fukui, Japan
Masafumi Kubota, University of Fukui Hospital, Japan

Disorders of the nervous system can cause paraplegia, which prevents human mobility and decreases quality of life. A major therapeutic goal is to recover motor and sensory function in individuals who have sensory or motor impairments, due to an accident or illness, and to provide support for the performance of daily life activities. For this purpose, the authors developed a multi-functional system based on interference-driven electrical stimulation that can promote the recovery of sensory-motor functions. The interference-driven electrical stimulation method was developed using a mixed stimulation signal with a carrier wave at a frequency that has been shown to stimulate human muscle. The parameters of electrical stimulation were optimized using a grasp/open hand task and a flexion/extension foot task based on the brain activity following electrical stimulation. This chapter reports the experimental results of the effects of electrical stimulation on motor function and brain activity in partially paralyzed stroke patients during the three phases of stroke symptoms.
Chapter 20
A Neuromorphic Robot Vision System to Predict the Response of Visual Neurons

Kazuhiro Shimonomura, Ritsumeikan University, Japan

The author of this chapter describes a binocular robotic vision system that was designed to emulate the neural images of cortical cells under vergence eye movements. The robotic vision system is constructed by employing a combinational strategy of neuromorphic engineering and conventional digital technology. The system consists of two silicon retinas and a field programmable gate array (FPGA). The silicon retinas carry out Laplacian-Gaussian-like spatial filtering, mimicking the response properties of the vertebrate retina. The outputs of the silicon retina chips on the left and right cameras are transmitted to the FPGA. The FPGA receives the outputs from the two simple cell chips and calculates the responses of complex cells based on the disparity energy model. This system provides complex cell outputs tuned to five different disparities in real-time. The vergence control signal is obtained by pooling these multiple complex cell responses. The system is useful for predicting the neural images of the complex cells and for evaluating the functional roles of cortical cells in real situations.

Chapter 21
Biomedical Robotics for Healthcare

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Recently, a robotic system was developed in the biomedical field to support minimally invasive surgery. The popularity of minimally invasive surgery has surged rapidly because of endoscopic procedures. In endoscopic surgery, surgical procedures are performed within a body cavity and visualized with laparoscopy or thoracoscopy. Since the initial laparoscopic cholecystectomy was performed in 1987, the implications for endoscopic procedures have continuously expanded, and endoscopic surgery is currently the standard for an increasing number of operations. Advances in laparoscopic surgery have led to less postoperative pain, shorter hospital stays, and an earlier return to work for many patients. However, performing laparoscopic procedures requires several skills that have never been required for conventional open surgery. The surgeon needs to coordinate his/her eyes and hands and acquire a skillful manner using long-shaft instruments as well as mentally interpret a two-dimensional environment as a three-dimensional one. Because learning such skills is stressful for most surgeons, performing a laparoscopic procedure is more physically and mentally demanding than performing an open procedure.

Sustainable Materials and Techniques in Healthcare

Chapter 22
Recent Progress in Mechanically Biocompatible Titanium-Based Materials

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Mechanical and biological biocompatibility is important consideration for materials that are used as metallic implants. During the past two decades, many β-type titanium alloys composed of non-toxic and hypoallergenic elements with low Young’s moduli have been developed worldwide. Recently, the development of new titanium-based materials to improve the mechanical and biological biocompatibility of metallic implants has progressed under advanced concepts. This chapter focuses on the improvement of mechanical biocompatibility, and recent research topics on such material developments are reviewed.
Hydrogels are used as scaffolds for tissue engineering in vitro & in vivo because their three-dimensional network structure and viscoelasticity are similar to those of the macromolecular-based extracellular matrix (ECM) in living tissue. Especially, the synthetic hydrogels with controllable and reproducible properties were used as scaffolds to study the behaviors of cells in vitro and implanted test in vivo. In this review, two different structurally designed hydrogels, single-network (SN) hydrogels and double-network (DN) hydrogels, were used as scaffolds. The behavior of two cell types, anchorage-dependent cells and anchorage-independent cells, and the differentiation behaviors of embryoid bodies (EBs) were investigated on these hydrogels. Furthermore, the behavior of chondrocytes on DN hydrogels in vitro and the spontaneous cartilage regeneration induced by DN hydrogels in vivo was examined.

In this chapter, the authors discuss the fabrication and properties of calcium phosphate coatings on titanium (Ti) by radio-frequency (RF) magnetron sputtering. First, they address the necessity of surface modification of metallic biomaterials and the effectiveness of calcium phosphate coating. Next, they briefly review the processes used in the application of calcium phosphate coatings and present the effect of sputtering parameters on the phase and deposition rates of these coatings. Finally, the chapter discusses the performance of amorphous and crystalline (oxyapatite) calcium phosphate coatings on Ti based on in vitro and in vivo evaluations.

Section 2
Brain-Machine Interfaces for Healthcare

Information Technology and Healthcare

Chapter 25
Nursing in Integrative Medicine and Nurses’ Engagement in Caring-Healing: A Discussion Based on the Practice and Study of Music Therapy and Nursing Care for Patients with Neurodegenerative Disorders

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Shin’ichi Nitta, Tohoku University, Japan & Organization for Development of Integrative Medical Healthcare Systems – HAMANASU Music and Nursing Therapy Association, Japan
In 2008, the authors' team started an ongoing project to administer music therapy sessions for patients with neurodegenerative diseases. Studies were made conducted from the "caring" perspective to evaluate the effects of music therapy on the mental health of the patients (Inomata, 2008a, Inomata 2008b) and on the role of nurses in integrative medicine (Inomata, 2008c). On the basis of the findings from these studies, music therapy programs were designed and conducted to meet the different needs of various neurodegenerative diseases. This project was the first ever reported music therapy initiative undertaken as a multi-disciplinary collaborative work and in partnership with a patients' group (Saji, 2010). The findings from four years of running the project are summarized as follows: (1) Music therapy helped maintain/improve the QOL (Quality of Life) level of neurodegenerative disease patients, which would otherwise deteriorate with the progress of symptoms; (2) There was an improvement in the patients' psychological and spiritual health as exemplified by the expansion of consciousness and rebuilding of relationships; (3) The project increased the feeling of partnership among the multi-disciplinary team members; (4) Care providers shared values such as self-belief and respect for both the self and others; (5) Caring for patients' emotional side by being compassionate and staying with them and/or listening to them resulted in a stronger care provider-patient bond; (6) Nurses were engaged in the building a healing environment as "healers," and the patients found more hope in everyday life.

Chapter 26
Non-Contact Pulse Monitoring Using Live Imaging .................................................. 240
Yuji Ohta, Ochanomizu University, Japan
Miki Uchida, Ochanomizu University, Japan

In this paper, the authors describe a novel non-invasive technique for monitoring pulse rate using live imaging. This method is based on the finding that brightness of the skin varies with pulsation due to the effects of blood scattering. The technical methods for image capture and data processing are described. The mechanism of light reflection inside the skin is also described using a layer model consisting of stratum corneum, epidermis, and dermis. This non-contact measurement method can yield natural physiological data during regular daily activities, and thus appears suitable for in-home healthcare monitoring.

Chapter 27
A Human-Like Cognitive Computer Based on a Psychologically Inspired VLSI Brain Model ...... 247
Tadashi Shibata, The University of Tokyo, Japan

Despite the enormous computational power of current digital computers, they are still inferior to humans in many respects, such as in seeing events happening in front, perceiving and recognizing them by intuition and association, and making a decision to take an immediate action. Furthermore, it appears very unlikely that computers will become as intelligent as humans in these aspects by just advancing the current computer technologies in any traditional way. Something radically new must be introduced to the architecture and algorithms in computers. In this chapter, the author presents an approach for building a human-brain-like computing system based on the computing principles that can be learned from biology and psychology. The author is exploring a new paradigm in the hardware computing scheme adaptive to human-like intelligent information processing based on the state-of-the-art very large scale integration (VLSI) technology. To this end, the author developed a series of VLSI chips that are each dedicated to mimicking specific processes of the brain using digital, analog, and/or mixed-signal circuit technologies. Specific applications of this system for the perception of still and moving images are presented as illustrative examples.
Chapter 28
Computational Study of the Hemodynamics of Cerebral Aneurysm Initiation ........................................ 267
Yuji Shimogonya, University of Hyogo, Japan
Takuji Ishikawa, Tohoku University, Japan
Takami Yamaguchi, Tohoku University, Japan
Hiroshige Kumamaru, University of Hyogo, Japan
Kazuhiro Itoh, University of Hyogo, Japan

This chapter aims to present the authors' recent findings from studies on the computational biomechanics of blood flow in human arteries and its application to the hemodynamics of cerebral aneurysm initiation. They first briefly outline the techniques of computational fluid dynamics used in blood flow simulations of anatomically realistic artery models reconstructed from medical images acquired with CT or MRI. Then, the time course of the blood flow velocity field in the medical image-based model of a human internal carotid artery (ICA) is shown as a result of a pulsatile blood flow simulation with CFD techniques. Finally, the chapter presents an overview of the concept of a novel hemodynamic indicator for cerebral aneurysm initiation, the gradient oscillatory number (GON). The distribution of the GON for the medical image-based ICA model is also demonstrated.

Chapter 29
Automated Analysis of Nursery School Observations ................................................................. 278
Jien Kato, Nagoya University, Japan

This chapter introduces an ongoing project with the goal of measuring and analyzing children's behavior automatically. Some key technologies, including methodologies for acquiring data, tracking a target across different cameras over time, identifying individuals, activity recognition, interaction analysis, and behavior summarization for a target child are presented. Some encouraging results from a real system developed in a nursery school environment are also described. As these technologies enable the content-based retrieval, comparison, and summarization of large-scale observational data, they are applicable to various purposes, such as healthcare, diagnosis, and the assessment of children's development.

Complex Bioinformatics and Healthcare

Chapter 30
Sleep Monitoring System Equipped with a Flexible Non-Contact ECG, Respiration, and Body Motion Sensor ................................................................. 287
Masaaki Makikawa, Ritsumeikan University, Japan
Shima Okada, Ritsumeikan University, Japan
Yoshihisa Fujiwara, R&D Headquarters, SANYO Electric Co., Ltd., Japan
Masayasu Esaki, ESP-Planning Co., Ltd., Japan

This study focuses on non-contact ECG measurement technology and introduces a sleep monitoring system equipped with non-contact electrocardiogram (ECG) electrodes and a respiration/motion sensor. The non-contact ECG measurement can be attained using capacitively-coupled electrode technology. The ECG of a subject with nightwear, such as pajamas, can be measured using this technique because it measures the ECG through a capacitor formed between the electrode and the ECG signal source. Using this sleep monitoring system, various sleep conditions of the elderly can be monitored, and abnormalities can be identified, such as abnormal heart rate and sleep behavior, including ambulation and sleep apnea, without disrupting their sleep. In many industrialized countries, including Japan, society is rapidly aging, and there is increasing demand for a system that can monitor the sleep of the elderly in nursing homes.
and care facilities and those living alone at home and thus increase their quality of life. By connecting this system with the hospital information systems or electronic medical record system, medical support and care planning will be more efficient.

**Chapter 31**

Fusion Physiological Sensing System for Healthcare

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Mitsuhiro Ogawa, Teikyo University, Japan
Takehiro Yamakoshi, Kanazawa University, Japan
Ken-ichi Yamakoshi, Kanazawa University, Japan

In the super-aging society, daily healthcare monitoring has become increasingly emphasized as a possible approach for the early diagnosis and timely treatment of lifestyle-related diseases. A wide variety of information transfers and platforms have been developed for daily healthcare monitoring. Using these techniques, the commercially available devices for home healthcare are also networked. However, techniques for obtaining physiological information are unfocused, and in such a case, even useful data cannot be obtained even if the network system is applied. Given these considerations, the authors have investigated a new network system combined with new bioinstrumentation techniques, i.e., the fusion physiological sensing system and its applicability for the daily healthcare monitoring. In particular, as contributions towards the development of healthcare technology, two promising monitoring techniques, ambulatory and non-conscious physiological monitoring, have been developed. These methods can contribute to the fields of the personal healthcare, medical care, and rehabilitation through their fusion with information and communications technology. The utility of these systems are reported according to the results of practical use, in addition to the outline of the sensing techniques in this chapter.

**Chapter 32**

Molecular Network Analysis of Target RNAs and Interacting Proteins of TDP-43, a Causative Gene for the Neurodegenerative Diseases ALS/FTLD

Jun-Ichi Satoh, Meiji Pharmaceutical University, Japan

TAR DNA-binding protein-43 (TDP-43) is an evolutionarily conserved nuclear protein that regulates gene expression by forming a multimolecular complex with a wide variety of target RNAs and interacting proteins. Abnormally phosphorylated, ubiquitinated, and aggregated TDP-43 proteins constitute a principal component of neuronal and glial cytoplasmic and nuclear inclusions in the brains of patients with amyotrophic lateral sclerosis (ALS) and frontotemporal lobar degeneration (FTLD), establishing a novel clinical entity designated TDP-43 proteinopathy. Although increasing evidence suggests that the neurodegenerative process underlying ALS and FTLD is attributable to a toxic gain of function or a loss of cellular function of TDP-43, the precise molecular mechanisms remain largely unknown. Recent advances in systems biology enable us to characterize the global molecular network extracted from large-scale data of the genome, transcriptome, and proteome with the pathway analysis tools of bioinformatics endowed with a comprehensive knowledge base. The present study was conducted to characterize the comprehensive molecular network of TDP-43 target RNAs and interacting proteins, recently identified by deep sequencing with next-generation sequencers and mass spectrometric analysis. The results propose the systems biological view that TDP-43 serves as a molecular coordinator of the RNA-dependent regulation of gene transcription and translation pivotal for performing diverse neuronal functions and that the disruption of TDP-43-mediated molecular coordination induces neurodegeneration in ALS and FTLD.
Chapter 33
Modularity of Biochemical Networks ................................................................. 336
Hiroyuki Kurata, Kyushu Institute of Technology, Japan

To reveal the relationships between large-scale, heterogeneous biochemical networks and their associated functions, called design principles in biology, it is critically important to disintegrate the networks into topology- or function-based subnetworks to analyze the mechanism of how each subnetwork generates a specific biological function, and to synthesize them as the whole system in the same manner as engineering, where a variety of parts are assembled into functional machines. This synthesis and analysis approach can be carried out by a computer. In this review, the author describes several methodologies that serve to disintegrate biological systems into biologically meaningful modules, with practical consequences for systems biology studies.

Systems Biology and Healthcare

Chapter 34
Methods for the Analysis of Intracellular Signal Transduction Systems ..................... 347
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This chapter introduces some practical methods for the analysis of intracellular signal transduction systems. If a biological system is described by a linear ordinary differential equation, various analytical tools are available to elucidate a control mechanism for the system in question. However, few systematic methods are available for nonlinear systems in which it is more capable of wide application for practical problems to describe a biological phenomenon by nonlinear modeling. Here, three effective methods for nonlinear systems analysis are demonstrated with a practical example involving a large-scale nonlinear model that includes signal transduction pathways, nucleocytoplasmic shuttling, and both transcriptional and translational control. Two methods of metabolic control analyses (MCA) are explained; the classical type can be applied to static conditions, and the alternative method can be used to analyze dynamic properties, such as peak, duration, and integral of time-course responses. Unlike MCA that cannot be experimentally verified because of technical limitations, the authors next explain an analytical method with a large perturbation. Finally, they introduce a parameter sensitivity analysis and explain that, by changing input characteristics, such as amplitude and frequency, some analysis of robustness can be achieved.

Chapter 35
Quantitative Modeling of Neuronal Polarization .................................................... 354
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Biological phenomena are systematically controlled by various components. In addition to biological molecules, physical components such as length and force must play an important role, especially in cellular morphogenesis. Although a quantitative mathematical model is useful for understanding the underlying mechanism of biological phenomena, a model including the physical components is likely to become too complex to be designed mathematically. In the authors’ previous work, they proposed a quantitative mathematical model of neuronal polarization that is described by several simple equations and can reproduce a number of experimental observations. Based on that work, this chapter explains how the authors obtained a simple quantitative model from the complex processes of neuronal polarization.
Brain-Machine Interface and Rehabilitation

Chapter 36
Brain–Machine Interface Using Brain Surface Electrodes: Real-Time Robotic Control and a Fully Implantable Wireless System

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The brain-machine interface (BMI) enables us to control machines and to communicate with others, not with the use of input devices, but through the direct use of brain signals. This chapter describes the integrative approach the authors used to develop a BMI system with brain surface electrodes for real-time robotic arm control in severely disabled people, such as amyotrophic lateral sclerosis patients. This integrative BMI approach includes effective brain signal recording, accurate neural decoding, robust robotic control, a wireless and fully implantable device, and a noninvasive evaluation of surgical indications.

Communication Technology

Chapter 37
Preservation and Reproduction of Human Motion Based on a Motion-Copying System

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In this chapter, a novel method for preserving and reproducing human motion based on haptic technology is described. Haptic technology makes it possible to preserve and reproduce human motion using a paired master and slave system. Because it is possible to preserve motion information based on position trajectory and force input, future human support technology that will facilitate skill acquisition, physical rehabilitation will be developed and will facilitate personal adaptation, tele-communication, et cetera. Once human motions are preserved, it will be possible to process them for various applications. For example, being able to reproduce the speed and trajectory of motion will allow for adjustments that fit the desired function. As a result, the temporal and spatial coupling of perception and action can be attained. This type of physical extension technology based on haptics will be important for the future of human support in society.
Chapter 38
A Simple Web-Based Image Database System for Facilitating Medical Care in Dermatological Clinics

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In Japan, electronic health record systems are gradually becoming popular at large hospitals, but are not yet frequently implemented in clinics. This is due to both prohibitive costs and a lack of interest in checking electronic health records on the part of patients. Doctors also may be opposed to showing patients their health records, as it then may require a doctor to let patients observe images to check for improvement of symptoms at follow-up. In this study, the authors developed a database system of dermatological images accessible to both doctors and patients. In this system, doctors can photograph affected skin areas and tag the images with keywords, such as patient ID or name, disease or diagnosis, symptoms, affected bodily regions, and free wards. The images and keyword tags are transmitted to a database housed on an Internet server. The authors implemented this system on a smartphone for quick and easy access during medical examination and on a tablet terminal for patients to use while waiting in the clinic. Using the tablet terminal, a doctor and patient may check for improvement of symptoms together.

Chapter 39
Ecological Momentary Assessment Using a Mobile Phone

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The mobile phone has become a popular tool for providing information and capturing responses from different groups of people because of its technological features and portability. EMA (Ecological Momentary Assessment) is commonly used by health researchers to contemporaneously capture information regarding human experience. The authors proposed the use of a mobile EMA system as a supportive intervention to collect real-time patient data and to give back real-time advice. In this study, a mobile EMA system has been utilized by patients with a variety of conditions, including mood disorders, behavior disorders, and physical disorders. The real-time data collection included one or more pieces of information at each moment to improve understanding the causal mechanisms of disease. The effectiveness of real-time advice has been examined by comparing a mobile EMA system with and without this function. Patient compliance was high on average, at approximately 89%, and was higher, at approximately 93%, when advice was given. In several cases, the supportive intervention was shown to help patients improve their health conditions. However, the results were dependent on the patients' motivation, environment, and relationship with their doctor. The EMA data regarding advice given showed that symptoms tended to improve in most cases.

Compilation of References

About the Contributors

Index